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Posterior Pituitary Ectopia: An MR Feature of Pituitary Dwarfism

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Using high-field-strength, 1.5-T, high-resolution MR, we identified the following complex of neurohypophyseal abnormalities in each of five pituitary dwarfs: (1) severe hypoplasia or total absence of the infundibulum; (2) absence of the posterior pituitary bright spot in its normal location; and (3) a 3–8-mm tissue nodule at the median eminence exhibiting lipidlike signal on T1-weighted images. On the basis of its signal features and the clinical absence of diabetes insipidus in these patients, the median eminence nodule appears to represent an ectopic and functional posterior pituitary gland.

We propose that this anatomic derangement is the end result of a localized defect of developmental origin, possibly ischemic in nature, and involving principally the infundibular stem. Thus, human growth hormone deficiency could result from perinatal disruption of the peri-infundibular hypophyseal portal system, which in turn impairs anterior pituitary function through deprivation of direct delivery of crucial hypothalamic-releasing factors. Finally, we suggest that the trophic influence of continued axonal neurosecretion at the median eminence engages proliferation of rest cell pituicytes; a process that induces formation of an ectopic and functional posterior pituitary gland, complete with its characteristic bright spot.

Although the underlying cause of congenital pituitary dwarfism remains unproved, the current consensus of opinion is that a primary hypothalamic lesion probably accounts for this neuroendocrine disorder. An increased incidence of breech delivery and birth asphyxia among newborns who later develop pituitary dwarfism has prompted researchers to invoke an ischemic mechanism of injury that impairs hypothalamic function in the perinatal period [1, 2]. However, pathologic proof of hypoxic damage to the hypothalamus is lacking, and cross-sectional imaging techniques have thus far failed to identify an abnormality of hypothalamic tissue. Furthermore, pituitary dwarfs have not been reported to exhibit an increased incidence of motor deficits or basal ganglia disturbances, which might be expected from injury to bordering nervous tissue that shares a common vascular territory with the hypothalamus.

High-resolution CT is a well-established and widely accepted method of evaluating the parasellar region. However, more recent experience indicates that state-of-the-art MR is currently the imaging technique of choice for investigating patients with suspected pituitary-related endocrine disease [3–5]. Relative to MR, CT provides comparatively poor soft-tissue contrast resolution, and diagnostic results are often hindered by beam-hardening artifacts projected through the sellar contents. Despite these technical limitations, a recent report illustrates convincing CT evidence of both pituitary gland and stalk hypoplasia in pituitary dwarfs [2].

The improved spatial detail provided by high-resolution MR enables more thorough delineation and tissue characterization of bordering structures in and about the sella turcica. These diagnostic advantages provide more consistent and reliable documentation of the recently described pattern of hypoplasia encountered in pituitary dwarfs and disclose additional findings that might help to elucidate the underlying cause of this disorder. The inherently superior contrast provided by MR

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TABLE 1: MR Findings in Five Pituitary Dwarfs

Case No.	Age (years)	Gender	Hypothalamus	Median Eminence Nodule Size (mm)	Infundibular Stalk	Sella Volume	Anterior Pituitary Size	Intrasellar Posterior Pituitary Bright Spot
1	2	M	Normal	3	Hypoplastic	↓	↓	Absent
2	4	F	Normal	4	Hypoplastic	↓↓	↓	Absent
3	12	M	Normal	8	Absent	Normal	↓	Absent
4	13	M	Normal	4	Hypoplastic	↓	Slightly ↓	Absent
5	27	M	Normal	5	Hypoplastic	Normal	Slightly ↓	Absent

is especially advantageous in this location, owing to the juxtaposition of varied soft-tissue structures and fluid compartments, each with characteristically different biochemical constituents. While these tissue differences are only subtly represented on CT, the potential contrast differentials can be greatly amplified on MR through judicious selection of instrument parameters.

For instance, the presence of lipid material contained in the cytoplasm of pituicytes in the posterior lobe may impart the normal posterior pituitary gland with unique signal characteristics on MR, a feature that serves to greatly enhance contrast discrimination of the pars nervosa from the anterior pituitary gland on T1-weighted images [6, 7]. Recent subprimate studies suggest that pituicyte cytoplasm volume and lipid content directly parallel hypothalamic-neurohypophyseal secretory activity, in particular antidiuretic hormone (ADH) synthesis and release [8, 9]. Thus, MR can clearly depict the structural components of the neurohypophysis and possibly also monitor the status or functional integrity of neurosecretion. The latter advantage—that is, the potential of MR to trace certain biologic markers of endocrine activity—prompted us to apply this technique in the investigation of pituitary dwarfs.

Patients and Methods

Five patients, each with endocrinologically verified idiopathic pituitary dwarfism, were studied. There were four males and one female, ranging in age from 2 to 27 years (Table 1). Characteristic somatic features included: (1) delayed growth and/or short stature; (2) immature body proportions; (3) truncal obesity, and (4) typical wizened facial appearances. Laboratory tests revealed anterior pituitary hormonal deficits with human growth hormone (HGH) deficiency in each case. HGH levels were either abnormally low or low-normal in the resting state, but all failed to increase appropriately in response to a provocative challenge with insulin, arginine, or L-dopa. Significantly, diabetes insipidus was not observed in our patient group, indicating preservation of both normal hypothalamic ADH synthesis as well as neuroregulatory control of its release.

MR studies were performed on a 1.5-T superconducting unit.* Two-dimensional Fourier transformation, multislice spin-echo (SE) pulse sequences were used. In each patient, 3-mm-thick contiguous T1-weighted images (600/20) were acquired in both the coronal and sagittal planes. In-plane voxel dimensions of 0.78 mm × 0.78 mm were maintained using a 256 × 256 pixel acquisition matrix, combined with a 20-cm field-of-view. Either four or six data sets (excitations) were obtained, resulting in imaging times of approximately 10 and 15 min, respectively. In one patient, a supplemental T2-weighted image (2000/35,70) transaxial sequence was obtained using 5-mm section thickness and 2.5-mm interslice gap. The scan range was carefully adjusted to ensure incorporation of the median eminence nodule completely within the margins of a single-section location.

The images were carefully evaluated with attention focused on the architectural features and intrinsic signal characteristics of the hypothalamic-pituitary unit. The size of the sella turcica, pituitary gland, and infundibulum were assessed in proportion to body size. The hypothalamus was evaluated for evidence of anatomic derangement, hypoxic damage, or other lesions associated with a focal signal alteration. The location and size of the posterior pituitary bright spot was recorded and interpreted as the definitive site of hypophyseal (pars nervosa) development. The MR findings were then compared with the appearance of the parasellar structures in five age-matched patients with normal pituitary function and two patients with acquired neurohypophyseal dysfunction, one with isolated diabetes insipidus from eosinophilic granuloma and the other with posttraumatic panhypopituitarism and transient diabetes insipidus from stalk transection. The latter two cases were reviewed to corroborate the impression of posterior pituitary ectopia in the dwarf patients and to help elucidate the potential etiologic significance of this finding.

Results

In all five pituitary dwarfs, a hyperintense soft-tissue nodule was plainly visible at the infundibular apex on T1-weighted images. The nodules exhibited a rounded or ovoid configuration (with vertical orientation) and varied from 3 to 8 mm in diameter as detailed in Table 1. In each case, the midline nodule was contiguous with the undersurface of the median eminence. The juxtaposition of the nodule with the inferior aspect of the hypothalamus was consistently observed and was demonstrated well on both sagittal and coronal images, as illustrated in Figure 1.

Coincident with the presence of a nodule at the median eminence in each of these patients was the uniform and conspicuous absence of a posterior pituitary bright spot (on T1-weighted images) at its expected location in the posterior and inferior aspect of the sella turcica. The focal hyperintensity of fatlike signal occasionally noted to originate from the marrow space of the dorsum sella could be distinguished from posterior pituitary tissue. This distinction was based on demonstration of a curvilinear band of low-intensity signal from cortical bone (representing the anterior margin of the dorsum sella) interposed between the sellar contents and the dorsum marrow space. In one patient a T2-weighted transaxial se-

* Signa, General Electric Medical Systems, Milwaukee, WI.

quence was obtained. On these images the signal amplitude of the dorsum sella marrow space was identical to marrow or subcutaneous fat at other locations. The signal also decayed in a fashion similar to fat when comparing the first- and second-echo images. The same dual-echo sequence provided further evidence that the nodule at the median eminence represents posterior pituitary ectopia. Specifically, the nodule displayed increased signal relative to intraorbital or subcutaneous fat on both the proton-density-weighted and the T2-weighted images of the long TR sequence, as depicted in Figure 2. The qualitative pattern of signal behavior exhibited by the nodule (relative to marrow or fat on the T1-weighted, proton-density-weighted, and T2-weighted images) is virtually identical to that of normal posterior pituitary tissue [10].

The sella turcica was clearly hypoplastic in one patient and abnormally small in two other patients, each with the appearance of compensatory thickening of unpneumatized sphenoid bone and dorsum sella marrow space (Figs. 1 and 2). In all five cases, even when the size of the sella turcica was not volumetrically reduced, the intrasellar pituitary gland appeared hypoplastic and showed homogeneous signal characteristic of only anterior pituitary tissue.

The infundibular stalk beneath the nodule at the median eminence was indistinct and of narrow caliber in four patients and totally absent in one patient. In the latter case, conspicuous absence of the infundibulum was clearly documented on a transaxial image obtained between the level of the nodule at the median eminence and the hypoplastic pituitary gland (Fig. 3).

In each of the five pituitary dwarfs the intrinsic structural

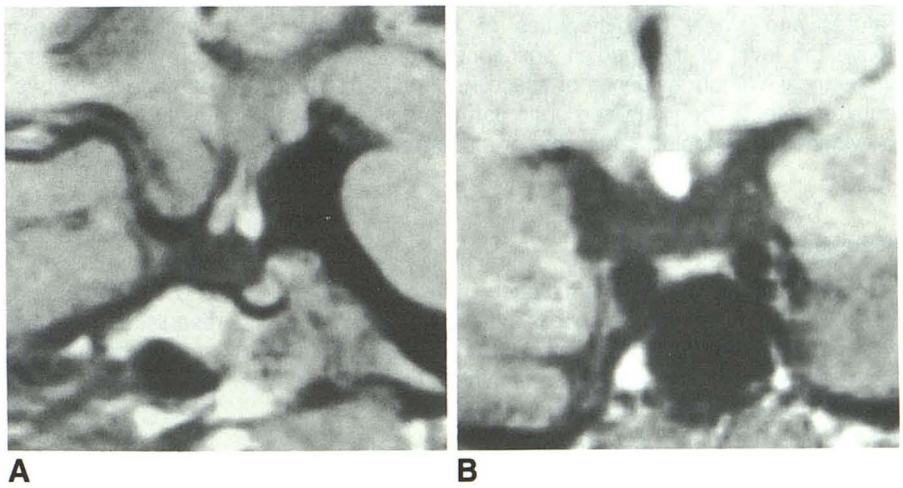

Fig. 1.—Case 2. Sagittal (*A*) and coronal (*B*) T1-weighted MR images depict 4-mm hyperintense midline nodule arising from undersurface of brain at median eminence immediately posterior to optic chiasm. An infundibulum cannot be seen on coronal view and is only faintly visible on sagittal image. Hypoplastic sella harbors small anterior pituitary gland with no evidence of posterior pituitary bright spot in its usual location. Also note compensatory thickening of dorsum sella and sphenoid body marrow space peripheral to hypoplastic sella.

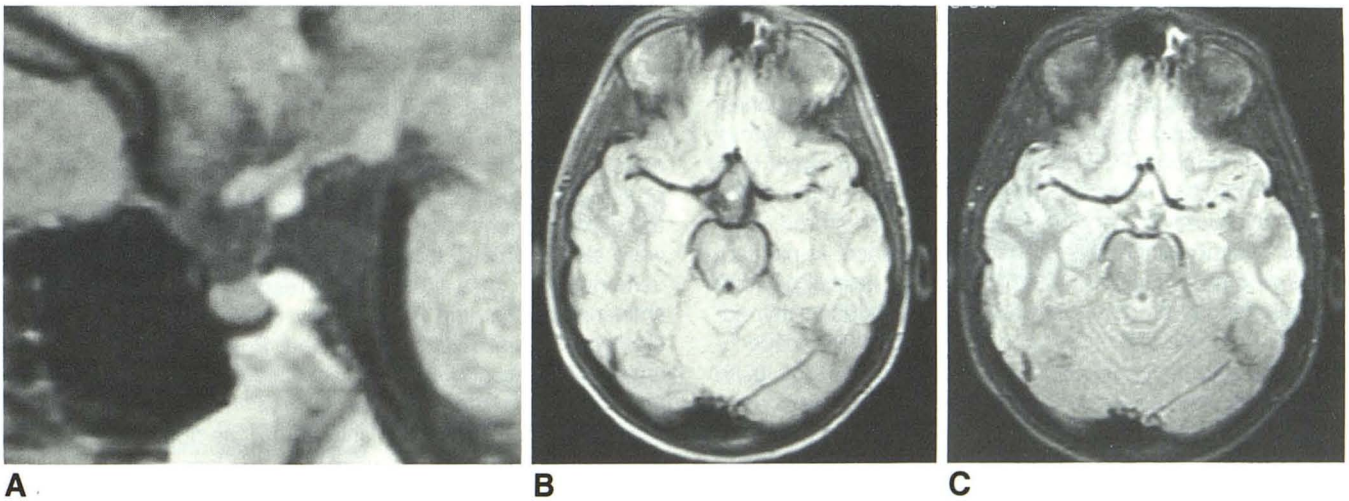

Fig. 2.—Case 4.

***A*, Ectopic posterior pituitary tissue at median eminence, as well as thickened dorsum sella marrow space, exhibit relative hyperintensity on sagittal T1-weighted MR image. On long TR dual-echo sequence (2000/35,70), entire dorsum decayed similarly to lipid signal of diploic marrow or subcutaneous/intraorbital fat.**

***B* and *C*, At slightly higher level on same transaxial sequence, median eminence nodule is displayed with increased signal relative to subcutaneous fat on both proton-density-weighted (*B*) and T2-weighted images (*C*), a finding characteristic of posterior pituitary tissue.**

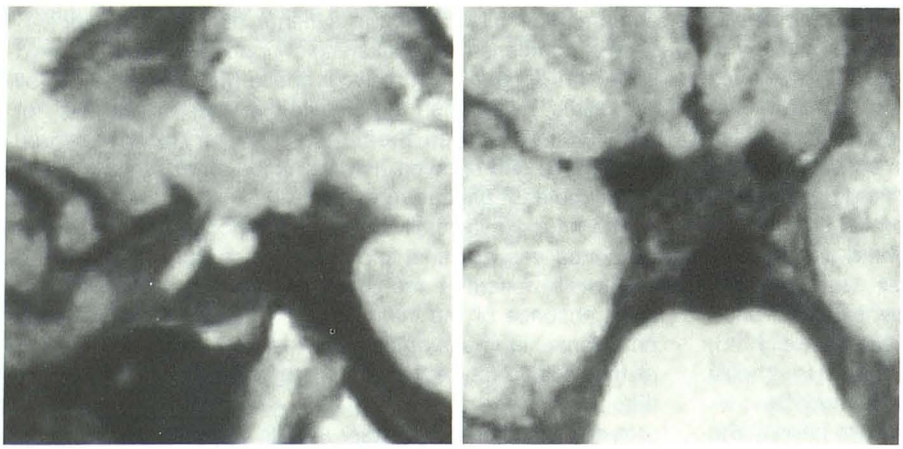

Fig. 3.—Case 3.
***A*, Midsagittal T1-weighted image shows no evidence of an infundibulum interposed between slightly hyperintense ectopic posterior pituitary gland at median eminence and shallow, hypoplastic sella below.**
***B*, Transaxial image through suprasellar cistern confirms absence of hypophyseal stalk (and peri-infundibular hypophyseal portal system). Prechiasmatic optic nerves are seen anteriorly, bordered by supraclinoid carotid arteries laterally. In the midline, at posterior aspect of cistern, flow void of basilar artery is surrounded by indistinguishable perifocal zone of dephased CSF.**

features and signal characteristics of the hypothalamus (above the level of the median eminence) were intact and symmetrical, without evidence of associated malformation or acquired defect. The visualized optic pathways also showed no evidence of hypoplasia, atrophy, or malformation.

Discussion

Congenital pituitary dwarfism caused by idiopathic deficiency of HGH accounts for approximately 10% of all cases of growth retardation [11]. Affected children manifest a 50–60% reduced velocity of growth and maintain immature body proportions that are usually recognized at 1–3 years of age. Other clinical features include truncal obesity, delayed secondary dentition, and, in later years, a characteristic facies with fine wrinkles about the eyes and mouth, imparting a paradoxically wizened appearance. Once the disease is suspected, the diagnosis is established by radioimmunoassay documentation of low HGH levels that fail to increase after a provocative challenge with insulin, arginine, or L-dopa. Besides HGH deficiency, additional anterior pituitary hormones, including adrenocorticotropic hormone ACTH and thyroid-stimulating hormone TSH, are measurably low in about one-half of all pituitary dwarfs. In many of these patients, the reserve levels of these hormones produced and stored in the anterior pituitary gland are normal. For instance, in pituitary dwarfs who also manifest hypothyroidism, a normal pituitary TSH reserve can be demonstrated by administering thyroid-releasing hormone (TRH), a response that has led to speculation of a hypothalamic origin of this disorder [12]. In an attempt to support this hypothesis, the possibility of perinatal asphyxia, or a vascular event, has been offered as a mechanism of injury that might result in hypoxic damage with resultant functional impairment of the hypothalamus in these patients. In fact, the occurrence of difficult deliveries, especially breech presentations, complicated by asphyxia and low Apgar scores, has been reported in over 50% of children who later prove to have pituitary dwarfism [1, 2].

The high incidence of birth stress in conjunction with endocrine tests indirectly suggestive of hypothalamic dysfunction would appear to support a theory of underlying hypoxic damage to the hypothalamic regulatory centers. Accordingly, many endocrine authorities currently favor a primary hypothalamic lesion as the likely cause of idiopathic hypopituitary dwarfism [12–14].

There is no conclusive evidence, however, that an ischemically induced hypothalamic defect initiates the endocrine failure that leads to pituitary dwarfism. High-resolution CT and MR imaging techniques, which in combination provide exquisite sensitivity for detection of ischemic changes, have so far failed to identify an intrinsic lesion in the hypothalamus of pituitary dwarfs. Direct evidence of such pathology is lacking as well.

A recent report of the CT findings in 12 pituitary dwarfs described by Inoue et al. [2] has shifted attention from the hypothalamus to the lower neurohypophysis as an apparent site of structural derangement. Four of the 12 patients failed to demonstrate evidence of either an infundibulum or a pituitary gland on high-resolution CT images. In an additional four patients, only a faintly visible infundibulum was seen. The remaining four patients showed a normal-to-small infundibulum and gland. Curiously, in none of these patients was a nodule of abnormal tissue identified at the median eminence or along the course of a hypoplastic stalk (corresponding to the ectopic bright spots shown on MR in our patients). We were also unable to locate a single reported instance of CT demonstration of a structure corresponding to the median eminence nodule that is so readily visible on MR in each of the five pituitary dwarfs we studied. Possibly, the CT attenuation of these nodular excrescences approximates and is masked by bordering CSF.

Bonneville et al. [15] has shown that the normal CT attenuation value of posterior pituitary tissue is less than 10. Thus, if indeed the median eminence nodule represents an ectopic posterior pituitary gland, its presence could plausibly escape detection on high-resolution CT, given the absence of mass effect and the lack of a significant contrast difference between the gland and the adjacent CSF.

The constellation of MR findings demonstrated in our pa-

tient group provides direct and convincing evidence of a structural defect and hints at the possibility of a functional disturbance localized to the infundibulum. This disturbance may represent the residua of arrested perinatal development with topologically aberrant proliferation of posterior pituitary tissue. An attempt to elucidate the potential pathophysiologic significance of the signal abnormalities encountered and the related etiologic implications is facilitated by first reviewing the normal functional anatomy of neurosecretion.

The hypothalamus modulates endocrine activity of the posterior and anterior pituitary gland through two anatomically distinct but physically juxtaposed pathways, referred to as the hypothalamohypophyseal tract and the hypophyseal portal system, respectively.

The hypothalamohypophyseal pathway consists of unmyelinated nerve fibers originating in the supraoptic and paraventricular nuclei of the hypothalamus and projecting to the posterior pituitary. The neurohypophyseal hormones ADH and oxytocin are synthesized in the supraoptic and paraventricular nuclei, bound to carrier proteins called neurophysin, and transported via axoplasmic flow to axon terminals in the posterior pituitary (Fig. 4).

The hypophyseal portal system consists of a vertically oriented tandem latticework of vascular channels that facilitates direct delivery of hypothalamic-releasing factors, including growth hormone-releasing factor (GHRF), from the tuberohypophyseal axon terminals in the median eminence to activator sites amidst the vascular sinusoids of the anterior pituitary (Fig. 5).

There appears to be ample evidence that the median eminence nodules identified on MR in our patients represent ectopic posterior pituitary lobe tissue, a conclusion upheld by the signal features and the clinical findings described herein. It is further supported by a few reports of autopsy findings in pituitary dwarfs that have appeared in older European literature [16–18].

In all five patients, the nodule at the median eminence was homogeneously hyperintense on the T1-weighted images. This appearance is identical to that of the pars nervosa at its expected location in the posterior sella (Fig. 6) and is similar to the hyperintensity of fat or clivus marrow. The possibility that a fatty congenital tumor (e.g., lipoma or dermoid) could account for the nodule was excluded on the basis of findings on the proton-density- and T2-weighted images. The increased signal of the nodule relative to fat or marrow was clearly demonstrated on these images (Fig. 2).

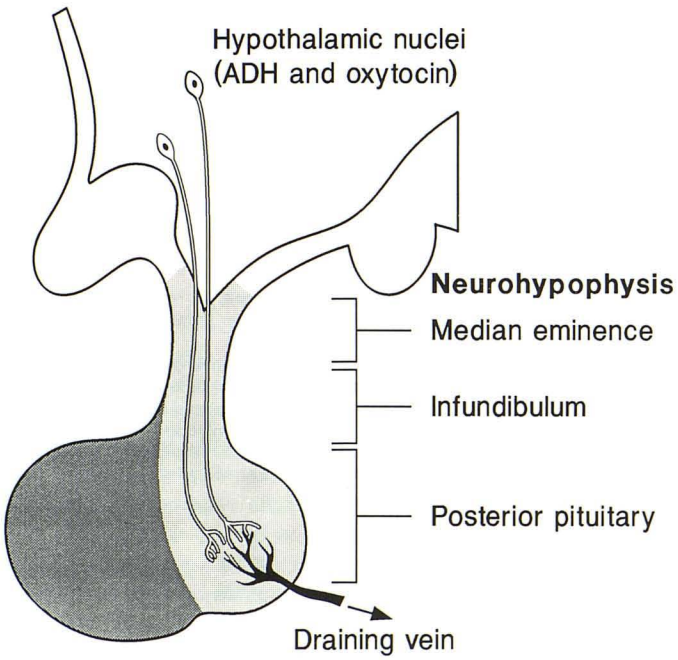

Fig. 4.—Hypothalamohypophyseal tract. Neurohypophyseal hormones ADH and oxytocin are synthesized in nerve cell bodies of supraoptic and periventricular nuclei. These octapeptides are bound to carrier proteins, packaged into neurosecretory granules, and transported via axoplasmic flow down through unmyelinated nerve fibers comprising the infundibular stem. Neurohypophyseal hormones are released into systemically draining veins in posterior pituitary lobe at axon terminals closely apposed to pituicytes (glial cell contribution of the posterior pituitary). The function of pituicytes is poorly understood, but proliferation of these cells and increased intracytoplasmic fat accumulation occurs in proportion to the activity of neurosecretion. Such fat accumulation may account for the hyperintensity of this portion of gland normally seen on T1-weighted images.

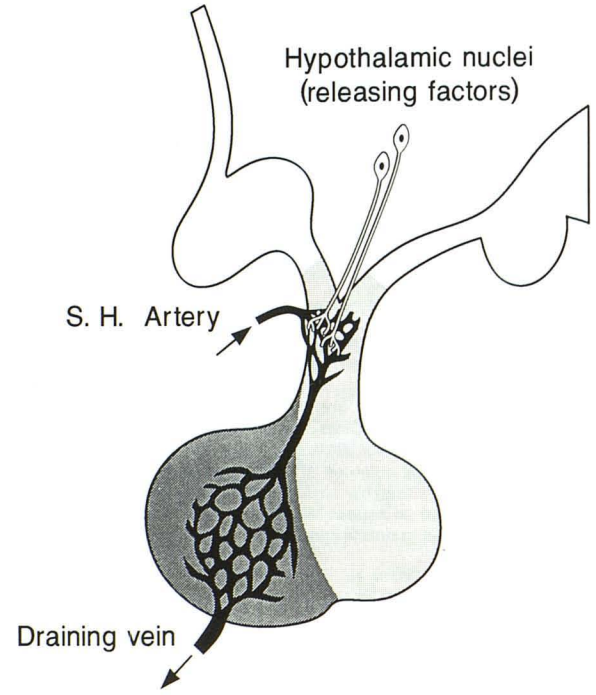

Fig. 5.—Hypophyseal portal system. Delivery of hypothalamic-releasing factors is a two-stage process. These chemotransmitter substances (including HGH-releasing factor) are synthesized in hypothalamic nuclei. They are conducted by axoplasmic flow to tuberohypophyseal nerve fiber terminals at median eminence. Here, neurosecretory material gains access to superior plexus of vertically oriented tandem latticework of peri-infundibular vessels. Blood flow carries neurosecretory products through long portal veins to inferior plexus. At activator sites amidst vascular sinusoids of anterior pituitary, hypothalamic-releasing factors stimulate release of systemically active anterior pituitary hormones produced in adenohypophysis. Normal endocrine activity of anterior pituitary, especially HGH secretion, is vitally dependent on direct transmission of releasing factors through this unique and delicate transportation link.

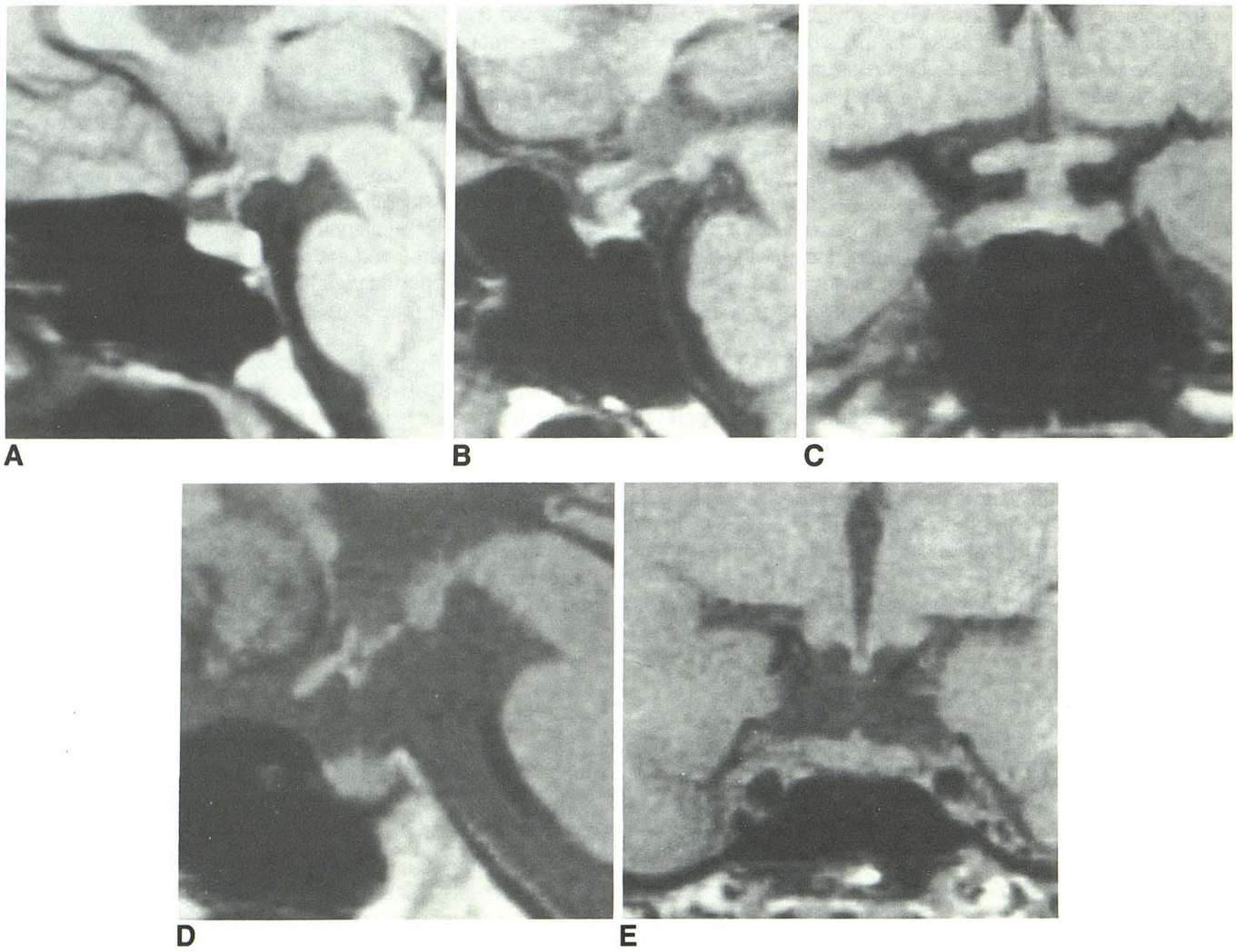

Fig. 6.—Normal sella and two examples of acquired diabetes insipidus with disappearance of posterior pituitary bright spot.

***A*, Sagittal T1-weighted image of sella in normal volunteer. Relative hyperintensity characteristic of normal posterior pituitary tissue is clearly demonstrated posteriorly in sella, behind adenohypophysis, which is isointense with neural tissue.**

***B* and *C*, Eosinophilic granuloma in patient with diabetes insipidus (sagittal and coronal T1-weighted images). Granulation tissue surrounds and constricts infundibulum. Conspicuous absence of posterior pituitary bright spot implies interference with hypothalamohypophyseal tract.**

***D* and *E*, Posttraumatic stalk transection in patient with transient diabetes insipidus and persistent panhypopituitarism (sagittal and coronal T1-weighted images). Segmental absence of stalk is seen in both projections, indicating disruption of both hypothalamohypophyseal tract hypophyseal portal system. Only dorsum sella marrow signal is seen posteriorly, without evidence of posterior pituitary bright spot. Proximal (ectopic) development of a bright spot was not observed on repeat MR after selective recovery from diabetes insipidus, suggesting a loss of ability to induce rest cell pituicyte proliferation at median eminence in adults (unlike the pattern observed in congenital pituitary dwarfism).**

The clinical absence of diabetes insipidus in our patient group implies preservation of normal hypothalamic synthesis of ADH. Axoplasmic transport of this neurophysin-bound octapeptide, and homeostatic control of its release, militates against the likelihood of a hypothalamic lesion.

Two recent MR reports assert that the hyperintensity of the normal pars nervosa on the T1-weighted image is attributable to a proposed short T1 time constant of the neurohypophyseal neurosecretory material (ADH/neurophysin complex) [5, 10]. It has also been shown that sectioning or ligation of the infundibulum in experimental animal models causes the secretory products of the neurohypophysis to accumulate proximally [19]. An obviously appealing explanation for the signal intensity of the median eminence nodule, then, is that it is due to ADH/neurophysin accumulation in ectopic posterior pituitary tissue. Although we agree that continued ADH neurosecretory activity is closely related to the hyperintensity of both normal location and ectopic posterior pituitary tissue on T1-weighted images, we suggest that the mechanism is only indirect, and the premise that the bright spot represents ADH/neurophysin may be premature.

An alternative explanation to account for the size and signal intensity of the bright spot is that it is governed by the glial cell component of the neural lobe; specifically, the intracellular lipid of pituicytes. Although pituicytes do not appear to participate directly in hormone synthesis, several studies suggest

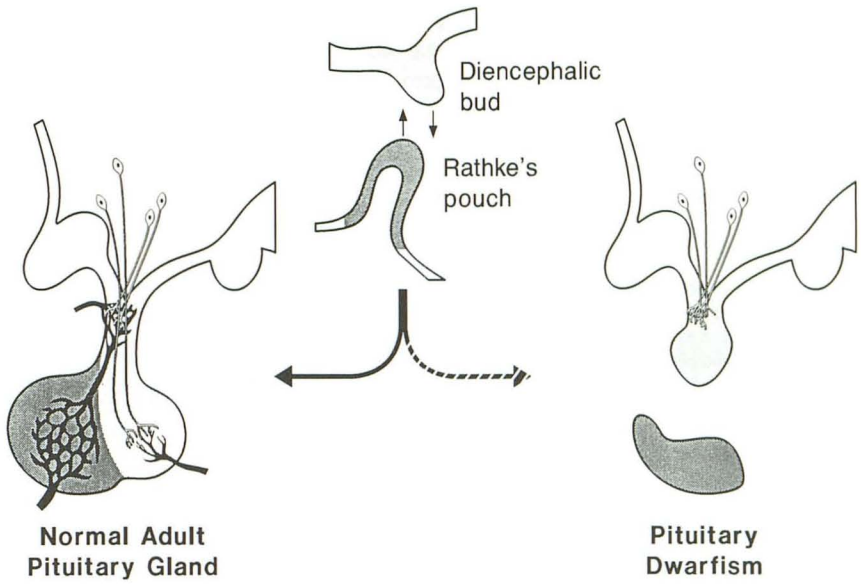

Fig. 7.—Proposed defect in pituitary dwarfism. Embryologic anlage of definitive pituitary gland consists of contributions from two distinct primordia. The diencephalic bud, a downward growth of neuroepithelium, gives rise to neurohypophysis and lends structural support for hypophyseal portal system. This vascular structure normally provides an important transport link to upward growth of buccal endoderm (Rathke pouch), which becomes the anterior pituitary. Perinatal occlusion of hypophyseal portal system would account for anterior pituitary hormone deficits that occur in pituitary dwarfism in association with stalk hypoplasia or atresia and ectopic proliferation of posterior pituitary tissue (see Discussion).

that they may have an important role in ADH or oxytocin secretion from the neurohypophysis. For example, pituicyte proliferation and intracytoplasmic fat accumulation have been demonstrated in a variety of physiologic conditions known to stimulate ADH release [8, 9]. One of our co-authors has produced similar results in a dog model and clearly demonstrated an ADH-stimulated increase in intracytoplasmic lipid in pituicytes on electron microscopy [7].

Because the median eminence nodules appear to represent posterior pituitary ectopia on the basis of MR and clinical findings, surgical correlation was never considered in our patients. As mentioned above, several isolated reports have provided gross pathologic and histologic documentation of the occurrence of posterior pituitary ectopia (referred to as "dystopia") in pituitary dwarfs, occasionally in conjunction with atresia or hypoplasia of the stalk [16–18]. The lesions are described as grayish-pink nodules (similar in size to those we encountered on MR) discovered at the base of the brain, where they are attached to the median eminence or a segment of hypoplastic stalk. These observations led us to conclude that the tissue nodules situated at the median eminence in juxtaposition to an atretic or hypoplastic infundibulum do in fact represent ectopic posterior pituitary tissue in our patients.

Our initial results in this small patient group also led us to propose a developmental basis for pituitary dwarfism. Embryologically, the anterior pituitary develops independently from the neurohypophysis, arising from an upward invagination of buccal endoderm (Rathke pouch). The adenohypophysis is a glandular structure devoid of neurosecretory nerve fibers. Hypothalamic control is mediated by the influence of physiotrophic-releasing factors or hormones. These chemotransmitter substances are transported from tuberohypophyseal axon terminals in the median eminence through the hypophyseal portal system (vascular component of the stalk) directly to the anterior pituitary, thereby governing release of adenohypophyseal hormones, including HGH (Fig. 5). Impaired function of this crucial neurohumoral control mechanism might logically result from any congenital or acquired lesion that interferes with the vital transportation link subserved by this delicate vascular network. This network develops in close relationship to the infundibulum and is probably dependent on the more rigid stalk for structural support.

Disruption of neuroendocrine transport functions normally carried out by the infundibulum impairs downward axoplasmic flow of neurohypophyseal hormones ADH and oxytocin in the central nerve fibers and downward vascular transport of hypothalamic-releasing factors in the peripherally situated hypophyseal portal system. Failure of these transport mechanisms is also responsible for panhypopituitarism, which follows traumatic or surgical sectioning of the stalk, as well as tumefactive or cicatricial compression of the stalk, such as from craniopharyngioma, germinoma, sarcoid, or eosinophilic granuloma (Fig. 6). The demonstration of an absent or severely hypoplastic infundibulum in pituitary dwarfs would likewise seem to preclude normal conveyance of neurosecretory products via this pathway.

The precipitating event that leads to the underlying structural defect might indeed be the result of a perinatal vascular accident that causes failed development, interruption, or occlusion of the hypophyseal portal pathway. This theory is supported by the known increased frequency of perinatal asphyxia in these patients, as alluded to earlier.

The onset of HGH deficiency in the perinatal period is consistent with the observation that pituitary dwarfs develop normally in utero and usually achieve normal birth weights. Hypothalamic regulation begins to stimulate anterior pituitary HGH secretion at 17–18 weeks gestation [20]. In most cases, normal homeostatic control appears to continue uninterrupted until shortly after a difficult delivery, coincident with transient hypoxic stress and the potential for an acquired ischemic insult or vascular occlusion affecting the developing neurohypophysis and specifically causing obliteration of the hypo-

physeal portal system. We propose that after such an event, the trophic influence of continued axonal ADH/neurophysin secretion at neurohypophyseal nerve terminals near the median eminence engages proliferation of rest cell pituicytes; a process that induces formation of an ectopic, functioning posterior pituitary gland as shown in Figure 7.

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